IFW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

HASELEY ET AL. Atty. Ref.: 1498-168

Serial No. 10/567,410 Group: Unknown

Filed: February 6, 2006 Examiner: Unknown

For: METHOD FOR THE DETECTION OF ABNORMALLY GLYCOSYLATED PROTEINS

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June 21, 2006

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

SUBMISSION OF INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

Submitted herewith is a copy of the International Preliminary Report on Patentability issued in PCT/GB2004/003385 dated February 6, 2006, for the Examiner's consideration.

Respectfully submitted,

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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING TRANSMITTAL OF COPY OF INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (CHAPTER I OF THE PATENT COOPERATION TREATY)
(PCT Rule 44bis.1(c))

To:

BECKHAM, Robert, William
D/IPD Formalities Section
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MOD Abbey Wood #2218
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IPR FORMALITIES
23 FEB 2006
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Date of mailing *(day/month/year)*	
16 February 2006 (16.02.2006)	
Applicant's or agent's file reference	IMPORTANT NOTICE
P1366/WOD	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/003385	05 August 2004 (05.08.2004)	05 August 2003 (05.08.2003)

Applicant
THE SECRETARY OF STATE FOR DEFENCE et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Nora Lindner
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference P1366/WOD	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/GB2004/003385	International filing date *(day/month/year)* 05 August 2004 (05.08.2004)	Priority date *(day/month/year)* 05 August 2003 (05.08.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant THE SECRETARY OF STATE FOR DEFENCE		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 06 February 2006 (06.02.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Authorized officer Nora Lindner Telephone No. +41 22 338 89 65

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

1/2 PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/003385	05.08.2004	05.08.2003

International Patent Classification (IPC) or both national classification and IPC
G01N33/74, G01N33/76

Applicant
THE SECRETARY OF STATE FOR DEFENCE DSTL

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 13-17 (in part)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 13-17 (in part)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	12-14,19
	No:	Claims	1-11,16-18,20-23
Inventive step (IS)	Yes:	Claims	13,14
	No:	Claims	1-12,16-23
Industrial applicability (IA)	Yes:	Claims	1-12,18-23
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 13-17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

For the assessment of the present claims 13-17 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: STORRING P L ET AL: JOURNAL OF ENDOCRINOLOGY, vol. 150, no. 3, 1996, pages 401-412.

D2: KELLY LISA S ET AL: PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 43, March 2002 (2002-03), pages 1078-1079.

D3: US-B-6 461 8311 (SMALL DAVID HENRY ET AL) 8 October 2002 (2002-10-08)

D4: SKIBELI V ET AL: HEMATOPOIESIS, vol. 98, no. 13, 2001, pages 3626-3634.

D5: IIDA SHIN-ICHIRO ET AL: JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 16, 16 April 1999 (1999-04-16), pages 10697-10705.

1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of independent claims 1,16 and 18 is not new in the sense of Article 33(2) PCT.

1.1 The document D1 discloses (the references in parentheses applying to this

document):
A method of screening a sample for the presence of one or more abnormally glycosylated and expressed proteins (rEPO), comprising the steps of I) exposing said sample to more than 2 different lectins (D1, abstract; Table 1, Figure 3) and determining the extent of binding of said sample to said lectins and comparing this to the extent of binding of a control sample (e.g. uEPO). (Details of the method can be found in D1, page 402, left-hand column, last paragraph-page 403, left-hand column, first paragraph). The materials used in this method are considered to constitute the corresponding kit according to claim 18. Therefore, D1 anticipates claims 1 and 18.

1.2 The document D2 discloses (the references in parentheses applying to this document):
A method of screening a sample for the presence of one or more abnormally glycosylated and expressed proteins (ectopic hCG), comprising the steps of I) exposing said sample to more than 2 different lectins (D2, abstract) and determining the extent of binding of said sample to said lectins and comparing this to the extent of binding of a control sample (normal hCG). The method of D2 is carried out on urine samples and permits diagnosis of an acquired glycosylation disorder. The materials used in this method (e.g. an array of eleven lectins in combination with specific capture antibodies) are considered to constitute the corresponding kit according to claim 18. Therefore, D1 anticipates claims 1,16 and 18.

1.3 The document D3 discloses (the references in parentheses applying to this document):
A method of screening a sample for the presence of one or more abnormally glycosylated and expressed proteins (an abnormal form of acetylcholinesterase in Alzheimer diseases), comprising the steps of I) exposing said sample to more than 2 different lectins (example 2) and determining the extent of binding of said sample to said lectins and comparing this to the extent of binding of a control sample (samples from control subjects). The method of D3 is carried out on inter alia CSF samples and permits diagnosis of an acquired glycosylation disorder (Alzheimer). The materials used in this method (e.g. eight different immobilised lectins) are considered to constitute the corresponding kit according to claim 18. Therefore, D3 anticipates claims 1,16 and 18.

2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-12 and 16-23 does not involve an inventive step in the sense of Article 33(3) PCT.

2.1 Dependent claims 2-12,17 and 19-23 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the EPC with respect to inventive step, the reasons being as follows:
The incorporation of the features of claims 2-12,17 and 19-23 into independent claims 1,16 and 18, respectively, is either obvious from D1-D5 or falls within the knowledge and ability of a person skilled in the art.

2.2 The subject matter of independent claim 13 - in as far as it relates to the glycoprotein drug rhEPO (see item 4) - is considered to involve an inventive step in the sense of Article 33 (3) PCT for the following reasons:

The document D4 is regarded as being the closest prior art to the subject-matter of claim 13, and discloses (the references in parentheses applying to this document) the notion that the sugar profiles of human serum EPO and rhEPO differ to such an extent, that the detection thereof can be used to detect the misuse of EPO in sports (D4 abstract). D4 uses HPLC analysis of purified EPO molecules, from which the subject-matter of claim 13 differs in that two or more different lectins or antibodies are incubated with a non-purified sample. The technical effect thereof is that no purification step is needed and that the claimed method is more specific.

The problem to be solved by the present invention may therefore be regarded as the provision of a simplified method for determining use of a glycoprotein drug (rEPO) in a mammal. The solution is to incubate the sample with two or more different lectins or antibodies .

The solution proposed in claim 13 of the present application can be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:
The use of multiple lectins to discriminate between various isoforms of a glycoprotein drug (EPO) that are differently glycosylated, is well known from D1. The person skilled in the art trying to solve the above mentioned problem will however not be prompted to use the method of D1, since the method of D1 is

intended for the quality control of purified EPO samples and not for an analysis of a non-purified sample.

2.3 Claim 14 is dependent on claim 13 and therefore also fulfills the requirements of Article 33(3) PCT.

3 The subject matter of claims 1-12 and 18-23 is considered to be industrially applicable in the sense of Article 33(4) PCT

4 The subject matter of claims 13 and 14 is neither supported (Article 6 PCT) nor disclosed in the description (Article 5 PCT) over the whole scope claimed.

4.1 Claims 13 and 14 relate to all glycoprotein drugs, whereas support and disclosure can only be found in the application for rhEPO. The problem claims 13 and 14 try to solve depends on a differential binding to lectins of natural hEPO and exogenous rhEPO. No support and disclosure is given for any other glycoprotein drug as to the differential binding to lectins thereof with respect to their natural counterpart.